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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WANG, CHANG YU	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,294	MICHEL ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/2/09*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5,7,8 and 54-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,7,8 and 54-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/2/09 has been entered.

Status of Application/Amendments/claims

2. Applicant's amendment filed 7/2/09 is acknowledged. Claims 2, 4, 6, and 9-53 are cancelled. Claims 1, 54 and 55 are amended. Claims 56 and 57 are newly added. Claims 1, 3, 5, 7, 8, 54-55 and newly added claims 56-57 are pending in this application and under examination in this office action.

3. Any objection or rejection of record, which is not expressly repeated in this office action, has been overcome by Applicant's response.

4. Applicant's arguments filed on 7/2/09 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections/Objections Maintained

In view of the amendment filed on 7/2/09, the following rejections are maintained.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, 7, 8 and 54-57 are rejected under 35 U.S.C. 102 (b) as being anticipated by WO01/88104 (Carpenter. published Nov 22, 2001) as evidenced by Baumann et al. (Physol. Rev. 2001. 81:871-927). The rejection is maintained for the reasons made of record.

Claims 1, 5, 7, 8 and 54-57 as amended are drawn to a method of generating $O1^+$ and/or $O4^+$ oligodendrocytes comprising growing neurosphere (NS) cells in a culture medium that promotes differentiation of NS cells into $O1^+$ and/or $O4^+$ oligodendrocytes, said culture medium comprising one or more gp130 activators selected from the group consisting of CNTF, oconstatin-M (OSM) or IL-6, IL6R/IL6 chimera and IL-11 and wherein said culture medium specifically enhances differentiation into O1+ and/or O4+ oligodendrocyte lineage, thereby causing the NS cells to differentiate along the oligodendrocyte lineage into O1+ and/or O4+ oligodendrocyte lineage. Dependent claims 56 and 57 are further directed to the culture medium promotes myelinating activity and formation of large and highly branched O+ and/or O4+ oligodendrocytes exhibiting large myelin membranes.

On p. 8-10 of the response, Applicant argues that amended claims have overcome the rejection because independent claim 1 has been amended to recite "specifically enhancing differentiation into the O1+ and/or O4+ oligodendrocyte lineage, thereby causing the NS cells to differentiate along the oligodendrocyte lineage into O+ and/or O4+ oligodendrocytes. Applicant argues that the amended language in claim 1 requiring preferential differentiation excludes the teaching of Carpenter (WO01/188104) resulting in the mixture of cells. Applicant also argues that no example in Carpenter shows specific differentiation into oligodendrocytes because only about 13% mature cells were GalC positive (markers for oligodendrocytes). Applicant's arguments have been fully considered but they are not persuasive.

In contrast, the examiner asserts that Carpenter does teach the claimed method of generating $O1^+$ and/or $O4^+$ oligodendrocytes comprising growing neurosphere (NS) cells in a culture medium that promotes differentiation of NS cells into $O1^+$ and/or $O4^+$ oligodendrocytes because Carpenter teaches a method of differentiating oligodendrocytes comprising growing primate pluripotent stem (pPS) cells including human embryonic stem cells in the presence of a gp130 activator including CNTF as recited in instant claim 1 (see p. 3; p. 6; p.8, lines 2-p. 11; p. 19, lines 10-35, examples, p. 20-23 examples 1-3, in particular). Carpenter teaches a method of differentiating cells re-suspended from cell suspensions from embryoid bodies and embryoid bodies are neurosphere cells because embryoid bodies were isolated and cultured with the same procedures as the claimed NS cells, which are also derived from embryonic stem (ES) cells (see p. 19, lines 10-35, in particular). Applicant fails to demonstrate that the

cultured NS cells derived from the suspension of embryoid bodies are different from the NS cells of Carpenter.

In addition, as previously made of record, the instant specification fails to show that the claimed method only generates pure and homogenous O1+ and/or O4+ oligodendrocytes. It is known in the art that the cultured neural precursor cells or neurosphere cells differentiate into a cell mixture encompassing different neural cells including neural progenitor cells, mature oligodendrocytes, astrocytes and neuronal cells.

Note that the Carpenter's method uses the same claimed materials, the same active agents and the same active steps as in the claimed method of the instant claims. The instant claims do not encompass or claim different active materials and steps from those taught by Carpenter. If the active materials, agents and steps are identical, the results would be identical. The amended limitation in a wherein clause in independent claim 1 is simply to state an intended result and it does not change the result of using the same active materials and the same active steps. The instant claims are not limited to a different culture condition and also are not limited to generating different percentages of O1+ and/or O4+ oligodendrocytes from that of Carpenter. Note that

In *Hoffer v. Microsoft Corp.*, 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005), the court held that when a "'whereby' clause states a condition that is material to patentability, it cannot be ignored in order to change the substance of the invention." *Id.* However, the court noted (quoting *Minton v.Nat'l Ass'n of Securities Dealers, Inc.*, 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003)) that a "'whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.'" *Id.*< See MPEP § 2111.04.

Furthermore, the limitation of “one or more gp130 activators is the only growth or differentiation agent present in the culture medium” is interpreted as “the only growth or differentiation agent that activates gp130 present in the culture medium”. The culture medium in the claimed method encompasses more than one growth or differentiation agent, and the culture medium for culturing and differentiating NS cells in the Carpenter are identical to that of the instant; thus, the presence of CNTF in the culture medium of Carpenter would be the only agent that activates gp130, which meets the limitation as recited in instant claim 54. Moreover, the language “comprising" recited in instant claim 1 does not exclude other factors in the culture.

As previously made of record, as long as the cultured NS cells are cultured at the same conditions in the presence of CNTF (a gp130 activator) and the cultured cells differentiate into mature oligodendrocytes, which are O4+ and O1+ as evidenced by Baumann (see p. 875, 2nd col, 2nd -3rd paragraphs, in particular), the Carpenter's method anticipates the claimed method as recited in instant claims.

On p. 10 of the response, Applicant also argues that the neural precursor cells of Carpenter are not the neurospheres described in instant specification because Carpenter does not start with neurospheres (NS) cells as described by Zhang et al.. Applicant further argues that Carpenter does not teach the limitations recited in new claims 56 and 57. Applicant argues that Applicant's arguments have been fully considered but they are not persuasive.

In contrast, as previously made of record, Carpenter does teach NS cells because the NS cells of the instant claims are cultured under the same conditions as those of Carpenter, which are dissociated from cultured embryoid bodies. Carpenter teaches a method of differentiating cells re-suspended from cell suspensions from embryoid bodies and the embryoid bodies are neurosphere cells because embryoid bodies and neurosphere cells are cultured and are derived from embryonic stem (ES) cells (see p. 19, lines 10-35, in particular). Since the culture conditions of Carpenter are identical to those described in the instant specification on p. 11-14, the cells in the differentiation method of Carpenter are identical to the NS cells of the claimed method. Applicant fails to provide evidence to show that the NS cells or cells derived from embryoid bodies of WO01/88104 are different from the claimed NS cells. Note that

"Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. 'There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102.' In re Best, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA1977)." See MPEP § 2112 [R-3]

If the product set forth in a product-by-process claim appears to be the same as, or an obvious variant of a product of the prior art, the claim is unpatentable even though the prior art product was made by a different process. See *In re Marosi*, 710 F.2d 799, 218 USPQ 289 (Fed. Cir. 1983) and *In re Thorpe*, 777 F.2d 695, 227 USPQ 964 (Fed. Cir. 1985). See also MPEP § 2113.

In addition, the limitations of "promotes myelinating activity" and "formation of large and highly branched O+ and/or O4+ oligodendrocytes exhibiting large myelin membrane" recited in new claims 56 and 57 are inherent results of the culture method. If the claimed method that uses the same active materials and same active steps as in the Carpenter's method can result in the limitations of instant claims 56 and 57, the

culture method of Carpenter can also achieve the same results because the claimed method does not claim different active materials, steps or conditions. Note that

6. Claims 1, 3, 5, 7, 8, and 54-57are rejected under 35 U.S.C. 102 (b) as being anticipated by US Patent No. 6562619 (Gearhart et al. issued on May 13, 2003, priority Mar 31, 1998) as evidenced by Baumann et al. (Physol. Rev. 2001. 81:871-927). The rejection is maintained for the reasons made of record.

Claims 1, 3, 5, 7, 8 and 54-57 as amended are drawn to a method of generating $O1^+$ and/or $O4^+$ oligodendrocytes comprising growing neurosphere (NS) cells in a culture medium that promotes differentiation of NS cells into $O1^+$ and/or $O4^+$ oligodendrocytes, said culture medium comprising one or more gp130 activators selected from the group consisting of CNTF, oconstatin-M (OSM) or IL-6, IL6R/IL6 chimera and IL-11 and wherein said culture medium specifically enhances differentiation into O1+ and/or O4+ oligodendrocyte lineage, thereby causing the NS cells to differentiate along the oligodendrocyte lineage into O1+ and/or O4+ oligodendrocyte lineage. Dependent claims 56 and 57 are further directed to the culture medium promotes myelinating activity and formation of large and highly branched O+ and/or O4+ oligodendrocytes exhibiting large myelin membranes.

On p. 11-12 of the response, Applicant argues that Gearhart does not anticipate the claimed method because Gearhart does not teach amended limitations and does not disclose a culture medium to promote the preferential differentiation of

oligodendrocytes. Applicant argues that Gearhart does not teach neurosphere cells. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, the examiner asserts that Gearhart does anticipate the claimed method. As previously made of record, Gearhart teaches a method of differentiating oligodendrocytes comprising growing embryonic stem (pPS) cells including mouse and human embryonic stem cells in the presence of a gp130 activator including IL-6 and IL-11 as recited in instant claims 1, 3, 5, 7 and 8 (see col. 28, example 6; col. 30, claims 1-28, in particular). Gearhart also teaches embryoid bodies and NS cells derived from embryonic stem (ES) cells as the NS cells recited in instant claim 1 (see co.. 29, lines 29-40; col.30, claim 9, In particular). The cells disclosed by Gearhart are re-suspended and passaged (col. 24-25, examples 1-2 and 6, in particular). Thus, the Gearhart's cells are identical to the NS cells in the claimed method. In addition, the culture medium in the Gearhart's method for differentiation contains IL-6 or IL-11, which is a gp130 activator as recited in instant claims 1 and 3 (see col. 28, example 6; col. 30, claims 1-28, col 14, line 27-col. 15, line 4 in particular). Thus, Gearhart's method anticipates the claimed as recited in instant claims.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 54 and 57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention. The rejection is maintained for the reasons made of record and as follows.

On p. 13 of the response, Applicant argues that the language of claim 54 clearly specifies that the culture medium does not have other growth factors in it and the specification also defines such claim language. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, the culture medium itself contains a lot of growth agents to maintain and promote cell survival. For example, the culture medium for NS cells described in the specification contains DMEM/F12, heparin, FGF-2, insulin, transferring, putrescine, selenite, progesterone (p. 14 & p. 29) and the differentiation medium contains DMEM/F12 with insulin, transferrin, putrescine, selenite, progesterone (see p. 29). These agents are the growth or differentiation agents. Thus, the gp130 activator cannot be the only growth or differentiation agent in the culture medium.

Accordingly, the recitation of "the gp130 activator is the only growth or differentiation agent present in the culture medium encompasses a broad range or limitation (i.e. culture medium itself containing a lot of growth agents) together with a narrow range or limitation that falls within the broad range or limitation (in the same claim), which is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). The recitation of "the gp130 activator is the only growth or differentiation agent present in the culture medium" is not consistent with the fact that the culture medium for growth or

differentiation of oligodendrocytes containing other factors for growth and differentiation in the culture medium. Thus, claim 54 is indefinite.

In addition, claim 57 is indefinite because the term "large and highly branched" and the term “large myelin membrane” in claim 57 is a relative term which renders the claim indefinite. The term "large or highly branched" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Applicant fails to set forth the metes and bounds of how much branching would be considered as “large and highly branched” or “small and less branched", and what size of the myelin membranes would be considered “small” or large membranes and thus would be within the definition of “large and highly branched” or “large myelin membranes” as recited in instant claim 57. Since the metes and bounds cannot be determined, it is not clear to a skilled artisan as to what size of oligodendrocytes with myelinating activity would be large and highly branched and would exhibit large myelin membranes. Thus, claim 57 is indefinite.

Conclusion

8. NO CLAIM IS ALLOWED.

9. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chang-Yu Wang, Ph.D.
August 27, 2009

/Chang-Yu Wang/
Examiner, Art Unit 1649